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**A small molecule primes embryonic stem cells for differentiation.**

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**Authors:** Shoutian Zhu, Heiko Wurdak, Jian Wang, Costas A Lyssiotis, Eric C Peters, Charles Y Cho, Xu Wu, Peter G Schultz

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**Public Summary:**

Embryonic stem cells (ESCs) are an attractive source of cells for disease modeling in vitro and may eventually provide access to cells/tissues for the treatment of many degenerative diseases. However, applications of ESC-derived cell types are largely hindered by the lack of highly efficient methods for lineage-specific differentiation. Using a high-content screen, we have identified a small molecule, named stauprimide, that increases the efficiency of the directed differentiation of mouse and human ESCs in synergy with defined extracellular signaling cues. Affinity-based methods revealed that stauprimide interacts with NME2 and inhibits its nuclear localization. This, in turn, leads to downregulation of c-Myc, a key regulator of the pluripotent state. Thus, our findings identify a chemical tool that primes ESCs for efficient differentiation through a mechanism that affects c-Myc expression, and this study points to an important role for NME2 in ESC self-renewal.

**Scientific Abstract:**

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